Remarks

Applicants request reconsideration of the above-referenced patent application.

I. Claim Amendments

Claims 1, 4, 5, 8, 9, 12-24, 26, and 27 are pending. Applicants have amended claims 1 and 23. All the claims, including the amendments, are shown in the previous section. Applicants submit that the amendments do not introduce any new matter. Specifically:

Claims 1 and 23 have been amended to recite the disorders listed in Applicants' specification at, for example, Paragraph 37 on pages 12-13.

Claims 1 and 23 have been amended to recite the composition concentration as an amount effective for the "treatment" (rather than "treatment and/or prophylaxis") of a COX-2 mediated ophthalmic disorder.

Claim 23 has been amended to be directed to "treating" (rather than "treating or preventing") a COX-2 mediated ophthalmic disorder.

Other amendments rephrase the claims, remove redundancies or unnecessary terms, or correct grammatical or obvious errors. Applicants submit that such amendments are permissible under MPEP §2163.07.

Applicants reserve the right to pursue any canceled subject matter and/or any other subject matter disclosed in this application in one or more later-filed divisional and/or continuation applications.

II. Response to rejection of claims 23, 24, 26, and 27 under 35 U.S.C. §112 (first paragraph)

Claims 23, 24, 26, and 27 have been rejected under 35 U.S.C. §112 (first paragraph) for failure to enable their entire scope. Applicants request withdrawal of this rejection.

The Office action raises two concerns with respect to the claims. First, the Office action objects to the recitation of COX-2 mediated ophthalmic disorders generally, which includes disorders not specifically listed in Applicants' specification. According to the Office action, Applicants' specification does not provide evidence that Applicant knew of such unspecified diseases. Applicants submit that U.S. patent law does not require Applicants' specification to list

every possible specific disorder falling within their claimed genus of disorders. Nevertheless, claim 23 has been amended to further define the COX-2 mediated disorder by reciting the specific disorders listed in Paragraph 37 on pages 12-13, thus mooting the Examiner's concern. The Office action also objects to the claims reciting "prevention" in addition to "treatment" of such disorders. Claim 23 has been amended to remove the "prevention" language, thus mooting the Examiner's concern. Thus, Applicants submit that the amendments have mooted both concerns raised in the Office action as to claim 23. Applicants have amended claim 23 in an effort to expedite prosecution of this patent application, and make no further representation as to the merit of this rejection.

Claims 24, 26, and 27 directly or indirectly depend from claim 23. Applicants therefore submit that these claims satisfy 35 U.S.C. §112 (first paragraph) for at least the same reasons as claim 23.

III. Response to rejection of claims 1, 4-5, 8, 9, 12-24, 26, and 27 under 35 U.S.C. §103(a)

Claims 1, 4-5, 8, 9, 12-24, 26, and 27 have been rejected under 35 U.S.C. §103(a) as being unpatentable over WO 00/25771 in view of Davis et al. (U.S. Patent 5,192,535) and Mazuel et al. (U.S. Patent 4,861,760). Applicants request withdrawal of this rejection.

Claim 1 is directed to a pharmaceutical composition for topical administration to the eye. The composition comprises a selective COX-2 inhibitory drug (or salt or prodrug thereof). In addition, the composition comprises an excipient ingredient that reduces the rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time of from about 2 to about 24 hours. As far as Applicants are aware, selective COX-2 ophthalmic compositions disclosed prior to Applicants' invention were not described as being resistant to removal from the eye by lacrimation, and, in particular, were not described as having an effective residence time of at least about 2 hours. It was Applicants, in accordance with this invention, who first recognized the advantages of such residence time. Applicants believe that these advantages arise out of multiple factors, including the following:

A. Low solubility of COX-2 inhibitory drugs. Most COX-2 inhibitory drugs have low water solubility. Thus, in aqueous compositions, such drugs are typically present as dispersed particles from which release is not instantaneous. Applicants believe that their novel residence time for such drugs allows more of the drugs to be released relative to prior ophthalmic compositions comprising selective COX-2 inhibitory drugs.

B. Need for sustained COX-2 inhibitory action. The dosage in the context of topical administrations to the eye is generally insufficient to lead to a therapeutically effective blood serum concentration. Thus, sustained COX-2 inhibition in this context is dependent on the COX-2 drug remaining *in situ* at the locus of application.

C. Lower dosages. By maintaining the COX-2 inhibitor drug at the site of application, the need for oral dosing of a COX-2 inhibitor drug is reduced or eliminated. This generally results in less COX-2 inhibitor drug being administered.

These advantages are discussed in Applicants' specification at, for example, Paragraphs 44-47 on pages 15-16.

WO 00/25771 discusses ophthalmic compositions containing a prostaglandin analogue and an anti-inflammatory agent. The anti-inflammatory agent is reported to reduce iridial pigmentation side effects during topical prostaglandin therapy for glaucoma. WO 00/25771 recites a list of anti-inflammatory agents, which includes celecoxib and rofecoxib. As acknowledged by the Office action, however, WO 00/25771 fails to teach, suggest, or provide motivation for a topical composition (and particularly a selective COX-2 inhibitor topical composition) that includes an excipient ingredient that reduces the rate of removal by lacrimation so that the composition has an effective residence time of from about 2 to about 24 hours. Given that WO 00/25771 is missing this disclosure, the subject matter of claim 1 cannot be *prima facie* obvious in view of WO 00/25771 alone. *See* MPEP §2143 ("[t]o establish a *prima facie* case of obviousness, . . . the prior art reference . . . must teach or suggest all the claim limitations.").

The subject matter of claim 1 also cannot be *prima facie* obvious in view of WO 00/25771, Davis et al., and Mazuel et al. For a combination of references to establish a *prima facie* case of obviousness, there must be a motivation to combine the teachings of the references. As noted in MPEP §2143:

> [t]o establish a *prima facie* case of obviousness, . . . there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

There is no such motivation for combining WO 00/25771 with Davis et al. or Mazuel et al. WO 00/25771, after all, provides no such motivation. As acknowledged in the Office action, WO 00/25771 fails to recognize a need for reducing the rate of removal of a selective COX-2 composition from the eye by lacrimation, and particularly fails to recognize a need for a residence time of at least about 2 hours. Because WO 00/25771 fails to recognize this need for increased residence time, one skilled in the art reading WO 00/25771 would have had no motivation from WO 00/25771 to use the teachings of Davis et al. or Mazuel et al. to increase residence time. It was Applicants --- not the authors of WO 00/25771 --- who first recognized a need for increased residence time for topical ophthamic compositions comprising a selective COX-2 inhibitory drug. Use of Applicants' discovery as motivation for combining the teachings of WO 00/25771, Davis et al., and Mazuel et al. consequently constitutes impermissible hindsight analysis. Given the absence of motivation for combining the teachings of the cited references, the subject matter of claim 1 cannot be *prima facie* obvious in view of WO 00/25771, Davis et al., and Mazuel et al.

Claims 4-5, 8, 9, and 12-22 directly or indirectly depend from claim 1, and therefore are patentable over the cited references for at least the same reasons as claim 1.

Claim 23 is directed to a method of treatment using the composition of claim 1. Thus, claim 23 is necessarily patentable over the cited references for at least the same reasons as claim 1.

Claims 24, 26, and 27 directly or indirectly depend from claim 23, and therefore are patentable over the cited references for at least the same reasons as claim 23.

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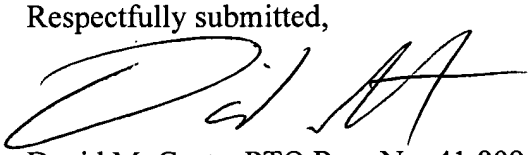
Applicants hereby request a 3-month extension to respond to the September 9, 2004 Office action, and are filing this amendment with a request for continued examination. Applicants have enclosed a check to cover the fee for the extension and request for continued examination. Applicants believe that they do not owe any additional fee in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **08-0750**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **08-0750**.

Applicants submit that the pending claims are in condition for allowance, and request that this application be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,



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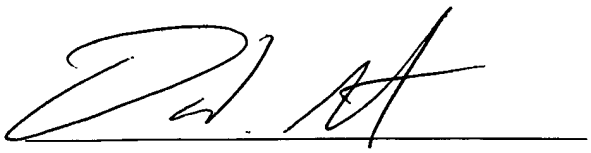
I certify that this correspondence is being deposited with the U.S. Postal Service on **March 9, 2005** with sufficient postage as first class mail (including Express Mail per MPEP §512), and addressed to **Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450**.



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